

Claims

1. A method for reducing vancomycin resistance in a vancomycin-resistant organism comprising:
introducing into the organism at least one anti-sense vancomycin resistance molecule under conditions to inhibit expression of a vancomycin resistance gene.
2. The method of claim 1, wherein the vancomycin resistant organism is selected from the group consisting of the Gram-positive bacteria, *Enterococcus faecalis* and *Enterococcus faecium*, and other Gram-positive bacteria such as *Staphylococcus species*, and *Streptococcus species*, to which these organisms have the potential of transferring resistance determinants.
3. The method of claim 1, wherein the vancomycin resistant organism is a Gram-positive bacteria.
4. The method of claim 3, wherein the Gram-positive bacteria is an enterococcus.
5. The method of claim 1, wherein the vancomycin resistant organism is selected from the group consisting of a VanA resistant organism, a VanB resistant organism, a VanC resistant organism, and a VanD resistant organism.
6. The method of claim 1, wherein the vancomycin resistant organism is a vanA resistant organism and the anti-sense vancomycin resistance molecule is selected from the group consisting of a *vanA* anti-sense molecule, a *vanR* antisense molecule, a *vanS* anti-sense molecule, a *vanH* anti-sense molecule, a *vanX* anti-sense molecule, a *vanY* anti-sense molecule and a *vanZ* anti-sense molecule.
7. The method of claim 1, wherein the vancomycin resistant organism is a VanB resistant organism and the anti-sense vancomycin resistance molecule is selected from the group consisting of a *vanRB* anti-sense molecule, a *vanSB* anti-sense molecule, a *vanYB* anti-sense molecule, a *vanW* anti-sense molecule, a *vanHB* anti-sense molecule, and a *vanXB* anti-sense molecule.

-33-

8. The method of claim 1, wherein the anti-sense vancomycin resistant organism is a VanC resistant organism.
9. The method of claim 1, wherein the vancomycin resistant organism is a VanD resistant organism and the anti-sense vancomycin resistance molecule is selected from the group consisting of a *vanD* anti-sense molecule, a *vanRD* anti-sense molecule, a *vanSD* anti-sense molecule, a *vanYD* anti-sense molecule, a *vanHD* anti-sense molecule, and a *vanXD* anti-sense molecule.
10. The method of claim 1, wherein the anti-sense vancomycin resistance molecule is a *vanA* antisense molecule selected from the group consisting of:
 - an antisense molecule that hybridizes to the complete *vanA* gene sequence; and
 - an antisense molecule that hybridizes to a conserved region of the *vanA* gene sequence.
11. The method of claim 10, wherein the *vanA* antisense molecule hybridizes to a conserved region of the *vanA* gene including from 10 to 30 nucleotides.
12. The method of claim 11, wherein the *vanA* gene encodes an enzyme and the *vanA* antisense molecule hybridizes to a region of the *vanA* gene which encodes an active site of the ligase.
13. The method of claim 1, wherein introducing the anti-sense vancomycin resistance molecule comprises contacting the vancomycin resistant organism with at least one vector comprising one or more "anti-sense vancomycin resistance molecules" under conditions to allow the vector to enter the organism and inhibit expression of one or more vancomycin resistance genes.
14. The method of claim 13, wherein the vector is selected from the group consisting of: an enterococcal shuttle vector, an enterococcal or any other species or strain of bacteriophage; the nucleic acid portion of a peptide nucleic acid molecule; an enterococcal conjugative transposon or a pheromone-responsive plasmid.

-34-

15. The method of claim 14, wherein the vector is an enterococcal shuttle vector.
16. The method of claim 13, wherein the vector contains a single copy of a *vanA* antisense molecule.
17. The method of claim 13, wherein the vector contains multiple copies of a *vanA* antisense molecule.
18. The method of claims 16 or 17, wherein the vector comprises a *VanR*-responsive promoter operatively coupled to the *vanA* antisense molecule.
19. The method of claim 1, wherein the anti-sense vancomycin resistance molecule is a *vanX* antisense molecule selected from the group consisting of:
 - an antisense molecule that hybridizes to the complete *vanX* gene sequence; and
 - an antisense molecule that hybridizes to a conserved region of the *vanX* gene sequence.
20. A method for reducing vancomycin resistance in a vancomycin-resistant organism comprising:
 - enhancing expression of a *vanH* promoter in the organism to an amount sufficient to reduce vancomycin resistance in the organism, wherein the *vanH* promoter is not operatively coupled to a vancomycin resistance gene of the organism.
21. The method of claim 20, wherein the *vanH* promoter is operatively coupled to an antisense vancomycin resistance molecule.
22. The method of claims 20 or 21, wherein the *vanH* promoter is contained on an enterococcus vector and enhancing expression comprises introducing into the organism an amount of the vector to express an amount of the *vanH* promoter sufficient to bind to phosphorylated *VanR* and thereby reduce vancomycin resistance in the organism.
23. The method of claim 20, further comprising co-administering into the organism an antisense vancomycin resistance molecule operatively coupled to a *vanH* promoter.

-35-

24. An isolated nucleic acid that hybridizes under stringent conditions to a nucleic acid molecule selected from the group consisting of SEQ ID NOs:1-13.
25. An isolated nucleic acid that hybridizes under stringent conditions to a nucleic acid molecule selected from the group consisting of SEQ ID NOs:5-13.
26. An isolated nucleic acid that hybridizes under stringent conditions to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs:5-10.
27. A vector comprising an isolated nucleic acid molecule of any of claims 24, 25 or 26.
28. The vector of claim 27, further comprising a *vanH* promoter operatively coupled to the isolated nucleic acid molecule.
29. An isolated vancomycin resistant organism comprising a vector of claim 27 or 28.